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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/912,818	07/24/2001	Daniel Pinkel	407E-914026US	8113

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EXAMINER	
FREDMAN, JEFFREY NORMAN	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 04/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/912,818	PINKEL ET AL.	
	Examiner	Art Unit	
	Jeffrey Fredman	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 March 2004* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *45-76* is/are pending in the application.

4a) Of the above claim(s) *72 and 73* is/are withdrawn from consideration.

5)☒ Claim(s) *45-67* is/are allowed.

6)☒ Claim(s) *68-71 and 74-76* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status

Claims 45-86 are pending.

Claims 45-67 are allowed (in view of the terminal disclaimer).

Claims 68-71, 74-76 are rejected.

Claims 72 and 73 are withdrawn from consideration.

Any rejection which is not reiterated in this action is hereby withdrawn as no longer applicable.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 68, 69, 71 and 74 are rejected under 35 U.S.C. 102(b) as being anticipated by Tsuda et al (Cancer Research (1989) 49:3104-3108).

Tsuda teaches method for detecting a copy number variation in a suspected breast cancer sample (see abstract) by detecting an amplification or gain of unique sequences (see abstract and page 3107, column 2, "Amplification of c-erbB2 was confirmed to be a factor indicating a poorer prognosis in breast carcinoma patients", also see figure 1, case A, where ear1 at position 17q21-22 is amplified) in at least one chromosomal region selected from the group consisting of:

on chromosome 17, about position q22 to about position q24 (see page 3104, column 2, "c-erbB-2 and one of the v-erbA-related genes, ear-1 are localized on chromosomes 17q21 and 17q21-22, respectively")

said method comprising:

(a) contacting a probe that binds selectively to a target polynucleotide sequence of said region with a nucleic acid sample prepared, directly or indirectly, from said suspected breast cancer sample, wherein said nucleic acid sample comprises said target polynucleotide sequence and said probe is contacted with said sample under conditions in which said probe fonns a stable hybridization complex with said target nucleic acid sequence (see page 3105, column 1, subheadings "Patients" and "DNA extraction and slot-blot hybridization analysis", and figure 1); and

(b) detecting said hybridization complex (see page 3105, column 1, subheading "DNA extraction and slot-blot hybridization analysis" and figure 1).

With regard to claim 69, Tsuda teaches a labeled probe (see page 3105, figure 1, "hybridized to ^{32}P-labeled probe DNA").

With regard to claim 74, Tsuda teaches extraction of primary tumor cells, which inherently comprises genomic DNA (see page 3105, column 1, subheading "DNA extraction and slot-blot hybridization analysis").

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and

the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 70, 75 and 76 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tsuda et al (Cancer Research (1989) 49:3104-3108) in view of Mullis et al (U.S. Patent 4,683,202).

Tsuda teaches the limitations of claims 68, 69, 71 and 74 as discussed above. Tsuda does not teach amplifying the DNA before detection or the use of cDNA.

Mullis teaches a polymerase chain reaction amplification method in which DNA is amplified prior to detection (see column 13, line 42 to column 14, line 17). Mullis further teaches the use of any DNA source, including cDNA (see column 5, lines 35-60). Mullis further teaches labeling of the sample DNA (see column 14, lines 8-17).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to amplify the sample of Tsuda as taught by Mullis since Mullis states

> "The method herein may also be used to enable detection and/or characterization of specific nucleic acid sequences associated with infectious diseases, genetic disorders or cellular disorders such as cancer. Amplification is useful when the amount of nucleic acid available for analysis is very small, as, for example, in the prenatal diagnosis of sickle cell anemia using DNA obtained from fetal cells. Amplification is particularly useful if such an analysis is to be done on a small sample using non-radioactive detection techniques which may be inherently insensitive, or where radioactive techniques are being employed but where rapid detection is desirable. (see column 13, lines 42-54)."

Thus, Mullis provides explicit motivation to amplify cancer related genes, such as the genes identified by Tsuda as associated with breast cancer, in order to perform rapid detection, which will minimize possible anxiety for breast cancer patients subject to the test, as well as more sensitive detection, to ensure that the cancer is detected even when the amount of material is very small. The practitioner in 1992 would have expected the PCR method of Mullis to function with a near absolute expectation of success.

Response to Arguments

6. Applicant's arguments filed November 17, 2003 have been fully considered but they are not persuasive.

First, because the rejection is maintained, the Markush election issue is not currently relevant.

Applicant argues that Tsuda does not apply because the erb-B2 gene is located at 17q12, not at 17q21. This argument is not persuasive for two reasons. First it does not appear to be factually correct. Second, it fails to address the claim language. Factually, the NCBI report on Erbb2 places the gene at both 17q11.2 and 17q21.1, as

shown on the attached sheet. Therefore, the gene expressly meets the claim limitation. Second, the language of the claim states "about 17q22". Since the specification does not define the term "about", the term permits a broad inclusion and 17q11 or 17q12 can certainly be deemed "about" 17q21. Therefore, the Tsuda reference remains applicable, even accepting Applicant's new information regarding the location of the erb-B2 gene.

Further, Applicant notes that the Ear1 gene, also amplified, is present at 17q21 but argues that 17q21 is not "about 17q22". If 17q21 is not "about" 17q22, then the term "about" has no weight whatsoever, which is not consistent with giving claims the broadest reasonable interpretation. Therefore, the association of breast cancer with the gain of the Ear1 gene also remains anticipatory.

Conclusion

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jeffrey Fredman
Primary Examiner
Art Unit 1637